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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,899	01/09/2001	Franciscus Antonius, M. Redegeld	4692US	1305

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/756,899	REDEGELD ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10,33 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 January 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11/26/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/26/03 has been entered.

2. Claims 1, 10, 33 and 34 are pending and are being acted upon in this Office Action.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 10, 33 and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a pharmaceutical composition consisting of a peptide consisting of SEQ ID NO: 1 and a pharmaceutically acceptable carrier or excipient for treating bronchial constriction, **does not** reasonably provide enablement for *any* pharmaceutical composition consisting of a peptide of SEQ ID NO: 1 and a pharmaceutically acceptable carrier or excipient for treating any disease state as set forth in claims 1, 10, 33 and 34. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a pharmaceutical composition consisting of a peptide consisting of SEQ ID NO: 1 and a pharmaceutically acceptable carrier or excipient for treating bronchial constriction wherein the peptide is present in an amount of 200 micrograms.

The specification does not teach how to make and use any pharmaceutical composition mentioned above for treating *any* disease because there is insufficient guidance as to the structure of a "peptide of SEQ ID NO: 1" in the claimed pharmaceutical composition since the length of peptide is ambiguous. If the peptide is intended to be close, it is suggest the term "consisting of" be use. Further, there is insufficient guidance as to which particular disease other than bronchial constriction to be treated with the claimed pharmaceutical composition.

Redegeld *et al*, of record, teach that free light chain is found in serum of a number of pathological conditions such as autoimmune multiple sclerosis, rheumatoid arthritis, neurological disorders (See abstract, in particular).

Hoppers *et al* teach that free light chain is found in urine of clinical relapse systemic lupus erythematosus (See abstract, in particular). Given the indefinite number of disease, there is insufficient in vivo working example demonstrating that the claimed pharmaceutical composition is effective for any autoimmune disease.

Rocken *et al* teach that animal experiments must determine whether specific k light chains are involved in T cell-dependent autoimmune diseases such as allergic encephalitis, inflammatory bowel disease, including contact hypersensitivity, psoriasis, rheumatoid arthritis, experimental allergic encephalitis (experimental model for multiple sclerosis).

Van Noort *et al*, of record, teach autoimmune diseases can be species and model-dependent (See entire document, pages 167-168, in particular). It is not clear the reliance on the animal model of BALB/C mice were skin-sensitized using picrychloride (PLC), dinitrofluorobenzene or oxazolone is appropriate for all autoimmune disease encompassed by the claims. Since the structure of the peptide is not enabled, it follows that the pharmaceutical composition consisting of said peptide is not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the

unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 11/26/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) a composition claim need not recite the intended use. (2) The specification provides a non-limiting list of exemplary diseases for example, page 4, lines 35 to page 5, line 15. (3) The office is directed to the list of non-exclusive list of US Patents and their respective claims, which claim pharmaceutical compounds without recitation of an intended use.

However, claim 10 recites a pharmaceutical composition for treating any disease. Although the specification provides a list of diseases that are associated with serum or spinal fluid concentration of free light chain of immunoglobulin, given the indefinite number of disease, there is insufficient in vivo working example demonstrating that the claimed pharmaceutical composition is effective for any disease other than bronchial constriction, including autoimmune disease.

Redegeld *et al*, of record, teach that free light chain is found in serum of a number of pathological conditions such as autoimmune multiple sclerosis, rheumatoid arthritis, neurological disorders (See abstract, in particular).

Hoppers *et al* teach that free light chain is found in urine of clinical relapse systemic lupus erythematosus (See abstract, in particular). Rocken *et al* teach that animal experiments must determine whether specific k light chains are involved in T cell-dependent autoimmune diseases such as allergic encephalitis, inflammatory bowel disease, including contact hypersensitivity, psoriasis, rheumatoid arthritis, experimental allergic encephalitis (experimental model for multiple sclerosis).

Van Noort *et al*, of record, teach autoimmune diseases can be species and model-dependent (See entire document, pages 167-168, in particular). It is not clear the reliance on the animal model of BALB/C mice were skin-sensitized using picrychloride (PLC), dinitrofluorobenzene or oxazolone is appropriate for all autoimmune disease encompassed by the claims.

In response to item 3, every case is examined on its own merit.

5. Claims 1, 10, 33 and 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of *any* pharmaceutical composition consisting of a peptide of SEQ ID NO: 1 and a pharmaceutically acceptable carrier or excipient for treating any disease state as set forth in claims 1, 10, 33 and 34.

The specification discloses only a pharmaceutical composition consisting of a peptide consisting of SEQ ID NO: 1 and a pharmaceutically acceptable carrier or excipient for treating bronchial constriction wherein the peptide is present in an amount of 200 micrograms.

With the exception of the specific pharmaceutical composition consisting of a peptide consisting of SEQ ID NO: 1 and a pharmaceutically acceptable carrier or excipient for treating bronchial constriction, there is insufficient written description about the structure associated with function of a peptide of SEQ ID NO: 1 in the claimed composition because the term "of" is ambiguous as to the length of the peptide. Further, the "disease state" in claim 10 encompasses autoimmune disease such as autoimmune multiple sclerosis, rheumatoid arthritis, neurological disorders. There is inadequate written description about the specific disease to be treated by the claimed pharmaceutical composition. Finally, given the lack of a written description of *any* additional representative species of peptide for treating additional representative species of disease as encompassed by the claims, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 1/2/03 have been fully considered but are not found persuasive.

Applicants' position is that claims have been amended.

However, claims 1 and 10 still recite a composition consisting of a peptide of SEQ ID NO: 1. The term "of" is ambiguous as to whether the peptide is intended to be open or close. The specification discloses only a pharmaceutical composition consisting of a peptide consisting

of SEQ ID NO: 1 and a pharmaceutically acceptable carrier or excipient for treating bronchial constriction wherein the peptide is present in an amount of 200 micrograms.

With the exception of the specific pharmaceutical composition consisting of a peptide consisting of SEQ ID NO: 1 and a pharmaceutically acceptable carrier or excipient for treating bronchial constriction, there is insufficient written description about the structure associated with function of a peptide of SEQ ID NO: 1 in the claimed composition because the term "of" is ambiguous as to the length of the peptide. Further, the "disease state" in claim 10 encompasses autoimmune disease such as autoimmune multiple sclerosis, rheumatoid arthritis, neurological disorders. There is inadequate written description about the specific disease to be treated by the claimed pharmaceutical composition. Finally, given the lack of a written description of *any* additional representative species of peptide for treating additional representative species of disease as encompassed by the claims, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 1, 10, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "**of** SEQ ID NO: 1" in claims 1 and 10 is ambiguous and indefinite because it is not clear the length of the peptide in the claimed composition. If the peptide is intended to be close, it is suggested that "consisting of" be used. If the peptide is intended to be open, it is suggests that "comprising" be used. One of ordinary skill in the art cannot appraise the metes and bound of the claimed invention.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 10, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Huang *et al* (J Clin Invest 99(4): 732-36, 1997; PTO 1449).

Huang *et al* teaches various compound such as a synthetic peptide AHWSGHCCL produced by a process comprising screening a series of compounds for it's capability to bind to an immunoglobulin light chain (LC) (See Methods, Table 1, page 734, in particular). The reference peptide is also identical to the claimed peptide of SEQ ID NO: 1, which has the amino acid sequence AHWSGHCCL (Table 1, in particular). The liquid associated with the reference peptide is considered a form of pharmaceutical carrier. Further, the reference peptide is in PBS and 2% TWEEN 20 just prior to adding to the wells of microplates coated with LCs (See page legend of figure 2, in particular). The reference peptide is useful for reducing the binding of the of immunoglobulin light chain to the THP (See Table 1 mic, IC_{50} mM, in particular). Claims 10 and 33 are included in this rejection because a composition is a composition irrespectively of its intended use.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 10, 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huang *et al* (J Clin Invest 99(4): 732-36, 1997; PTO 1449) in view Gennaro et al in Remington's Pharmaceutical Sciences, eighteenth edition, 1990, pages 1300-1329; PTO 892).

Huang *et al* teach various compound such as a synthetic peptide AHWSGHCCL produced by a process comprising screening a series of compounds for it's capability to bind to an immunoglobulin light chain (LC) (See Methods, Table 1, page 734, in particular). The reference peptide is also identical to the claimed peptide of SEQ ID NO: 1, which has the amino acid sequence AHWSGHCCL (Table 1, in particular). The reference peptide is useful for inhibiting the binding of the of immunoglobulin light chain to the THP (See Table 1 mic, IC_{50} mM, in particular).

The claimed invention differs from the teachings of the reference only by the recitation of a pharmaceutically acceptable carrier or excipient.

The claimed invention as recited in claim 34 further differs from the teachings of the reference only that the composition wherein the peptide is present in an amount of 200 microgram.

Gennaro *et al* teach various pharmaceutical acceptable carrier or excipient such as purified water, dextrin, sodium carbonate (See page 1301, page 1321, in particular). Gennaro *et al* teach that pharmaceutical carrier and vehicle are indifferent substances which are useful as solvents for active medicinals and primary importance for diluting and flavoring drugs. Gennaro *et al* teach that the best diluting agent is usually the best solvent for the drug (See page 1300, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to dissolve the peptide as taught by Huang et al in a pharmaceutically acceptable carrier as taught by Gennaro et al for a pharmaceutical composition as taught by Gennaro et al and Huang *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Gennaro et al teach that pharmaceutical carrier and vehicle are solvents for active medicinals and primary importance for diluting and flavoring drugs and the best diluting agent is usually the best solvent for the drug (See page 1300, in particular). Huang *et al* teach that the reference peptide is useful for the reference peptide is useful for inhibiting the binding of the of immunoglobulin light

chain to the THP (See Table 1 mic, IC_{50} mM, in particular). Claims 10 and 33 are included in this rejection because a composition is a composition irrespectively of its intended use. Claim 34 is included in this rejection because the concentration of peptide such as 200 micrograms is within the purview of one ordinary skill in the pharmaceutical art to adjust the dosage for the particular purpose. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 220 F2d 454,456,105 USPQ233; 235 (CCPA 1955). See MPEP § 2144.05 part IIA.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

15. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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